

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)RECEIVED
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(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 39153	FOR FURTHER ACTION See Form PCT/IPEA/416																									
International application No. PCT/FI 2003/000039	International filing date (day/month/year) 20.01.2003	Priority date (day/month/year) 18.01.2002																								
International Patent Classification (IPC) or national classification and IPC A61P 1/18, 9/00, 17/00, 31/04, C07H 15/04, 3/06, 1/00, A61K 31/702, 31/7028, 31/715, 31/726, A61P 1/04, 1/16, A61P 35/00, 37/00																										
Applicant Biotie Therapies Oyj et al																										
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>14</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> (<i>sent to the applicant and to the International Bureau</i>) a total of <u>12</u> sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (<i>sent to the International Bureau only</i>) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> <p>4. This report contains indications relating to the following items:</p> <table> <tbody> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </tbody> </table>			<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input checked="" type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input checked="" type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input checked="" type="checkbox"/>	Box No. VI	Certain documents cited	<input checked="" type="checkbox"/>	Box No. VII	Certain defects in the international application	<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application
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Date of submission of the demand 12.08.2003	Date of completion of this report 20.04.2004
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Per Renström/EÖ Telephone No. +46 8 782 25 00

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/FI 2003/000039

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:
- international search (under Rules 12.3 and 23.1(b))
 - publication of the international application (under Rule 12.4)
 - international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

- the international application as originally filed/furnished

the description:

pages 1-55 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

the claims:

pages _____ as originally filed/furnished

pages* _____ as amended (together with any statement) under Article 19

pages* 56-67 received by this Authority on 05-04-2004

pages* _____ received by this Authority on _____

the drawings:

pages 1-4 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

- a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. The amendments have resulted in the cancellation of:

- the description, pages _____
- the claims, Nos. _____
- the drawings, sheets/figs _____
- the sequence listing (*specify*): _____
- any table(s) related to the sequence listing (*specify*): _____

4. This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- the description, pages _____
- the claims, Nos. _____
- the drawings, sheets/figs _____
- the sequence listing (*specify*): _____
- any table(s) related to the sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/FI 2003/000039

Box No. II Priority

1. This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
 - copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
 - translation of the earlier application whose priority has been claimed (Rule 66.7(b)).
2. This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

The priority claim is considered valid and the documents cited in Box VI are therefore of no relevance.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/FI 2003/000039

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application
 claims Nos. 27-30, 33, 44-47; 1-3, 5-7, 9, 14-26, 34, 36-43, 48-51, 53, 65 pa

because:

- the said international application, or the said claims Nos. 27-30, 33, 44-47 relate to the following subject matter which does not require an international preliminary examination (*specify*):

See PCT Rule 67.1.(iv).: Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. See below. are so unclear that no meaningful opinion could be formed (*specify*):

Claims 1-3, 5-7, 9, 14-26, 34, 36-43, 48-51, 53 and 65 partly.

The initial phase of the search of the present claims 1-3, 5-7, 14-22, 25-26, 36-43, 48-51 and 65 revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine .../...

- the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for said claims Nos. _____
- the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- | | |
|----------------------------|--|
| the written form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
| the computer readable form | <input type="checkbox"/> has not been furnished |
| | <input type="checkbox"/> does not comply with the standard |
- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in the Annex C-bis of the Administrative Instructions.
- See Supplemental Box for further details.

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: III.

which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible. Consequently the search on which the examination is based was restricted to those parts of the application related to the contents of claims 4, 8, 10-13, 31-32, 35 and 52-64 and parts of claims 9, 23-24 and 34 (see below).

The expression "having Helicobacter pylori binding or inhibiting activity" in present claim 23 may relate to a number of different disorders and conditions which can not be clearly defined by this expression. The expression is therefore not an acceptable definition of for a second medical indication and claim 23 is not considered clear and concise according to Article 6 PCT. The search of claim 23 has been restricted to the term "helicobacter pylori" and the diseases mentioned in the present claim 26.

The expression "a substance identified according to claim 33" in the present claim 34 is not a clear and concise (Article 6 PCT) definition of chemical compounds, and has accordingly not been searched.

Claims 1, 4, 10, 38 and 41 - i.e. all independent substance claims except claim 9 - have a structure with the general formula $\text{Gal}(\text{NAC})_{r_2}\beta 4\text{Glc}(\text{A})_{q_2}(\text{NAC})_{r_3}$ in common (GlcA means that C6 in Glc is oxidized and derivatized to a uronic acid derivative). The indexes q₂, r₂ and r₃ are each independently 0 or 1, allowing for the following disaccharide sequences: GalNAc β 4Glc, Gal β 4GlcA, GalNAc β 4GlcA, GalNAc β 4GlcNAc, Gal β 4GlcANAc, GalNAc β 4GlcANAc, Gal β 4Glc and Gal β 4GlcNAc.

The present independent claim 9 includes five sequences that do not share this common structure, instead having the common structure Glc β 3GlcNAc β 4Glc. Claim 9 (former claim 8) was originally dependent on claim 1. The part of present claim 9 claiming said five sequences in themselves has not been searched or examined and is consequently not part of this international preliminary report.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/FI 2003/000039

Box No. IV Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:
 - restricted the claims.
 - paid additional fees.
 - paid additional fees under protest.
 - neither restricted nor paid additional fees.
2. This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
 - complied with.
 - not complied with for the following reasons:
4. Consequently, this report has been established in respect of the following parts of the international application:
 - all parts.
 - the parts relating to claims Nos. 1-26, 31-32, 34-43, 48-56, 61-65, see III.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/FI 2003/000039

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	4,10,12,61-64; 6-7,9,15-17,19,31-32, 34-35,37-43,48-56 partly	YES
	Claims	<u>1-3,5,8,11,13-14,18,20-26,36,65</u>	NO
Inventive step (IS)	Claims	4,10,12,61-64; 6-7,9 partly	YES
	Claims	<u>1-3,5,8,11,13-26,31-32,34-43,48-56,65</u>	NO
Industrial applicability (IA)	Claims	<u>1-26,31-32,34-43,48-56,61-65</u>	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Relevant documents (cited in the International Search Report):

D1: WO 0143751 A1 (A+ SCIENCE INVEST AB), 21 June 2001
(21.06.2001)

D2: Glycobiology, Volume 8, No. 4, 1998, Jonas Ångström et al, "The lactosylceramide binding specificity of Helicobacter pylori", pages 297-308

D3: STN International, File CAPLUS, CAPLUS accession no. 2001:118779, document no. 134:292940, Fujita, M. et al, "Ancorinosides B-D, inhibitors of membrane type 1 matrix metalloproteinase (MT1-MMP), from the marine sponge Penares sollasi Thiele", & Tetrahedron, (2001), 57(7), 1229-1234

D4: STN International, File CAPLUS, CAPLUS accession no. 1998: 534525, document no. 129:258636, Miura, Yoshiaki et al, "alpha-N-Acetylgalactosamine-capping of chondroitin sulfate core region oligosaccharides primed on xylosides", & Glycobiology (1998), 8(8), 813-819

D5: STN International, File CAPLUS, CAPLUS accession no. 1994:455685, document no. 121:55685, Yamamoto, Kazuo et al, "Interaction of Immobilized Recombinant Mouse C-Type Macrophage Lectin with Glycopeptides and Oligosaccharides", & Biochemistry (1994), 33(26), 8159-66

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: V.

D6: Anger H. et al, "Amidated pectins - characterization and enzymic degradation", Food Hydrocolloids (1988), 2(5), 371-9

D7: Kratchanov, C. et al, "Reaction of apple pectin with ammonia", International Journal of Food Science and Technology (1989), 24(3) 261-7

D8: STN International, File CAPLUS, CAPLUS accession no. 1989:171879, document no. 110:171879, Anger H. et al, "Amidated pectins - characterization and enzymic degradation", & Food Hydrocolloids (1988), 2(5), 371-9

D9: WO 02056893 A1 (CARBION OY), 25 July 2002
(25.07.02)

D10: STN International, File CAPLUS, CAPLUS accession no. 2002:390032, document no. 138:1587, Chandrasekaran, E. et al, "Biosynthesis of the carbohydrate antigenic determinants, Globo E, blood group H, and Lewis b: a role for prostate cancer cell alpha1,2-L-fucosyltransferase" & Glycobiology (2002), 12(3), 153-162

D11: WO 9827988 A1 (NUTRAMAX LABORATORIES), 2 July 1998
(02.07.98)

D12: EP 0354595 A1 (UNILEVER PLC), 14 February 1990
(14.02.90)

D13: US 3405120 A (TAKEHIKO KAWANO ET AL),
8 October 1968 (08.10.68)

D14: STN International, File CAPLUS, CAPLUS accession no. 1990:512024, document no. 113:112024, Pepop. Rep. China, "Method of production of D-aminogalactose hydrochloride for clinical analysis", & CN,A,1036386,19891018

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Previous supplemental box.

See Box III for information about which parts of the claims have not been searched or examined. See also Box VIII.

The present application is directed to Helicobacter pylori-binding substances comprising an oligosaccharide sequence of the general formula $\text{Gal}(\text{NAC})_{r_2}\beta\text{4Glc(A)}_{q_2}(\text{NAC})_{r_3}$, wherein GlcA is a glucuronic acid derivative and q2, r2 and r3 are each independently 0 or 1.

D1 (abstract; page 7, lines 3-10; Table II, pages 52-53; claims) describes Helicobacter pylori-binding di- and oligosaccharide substances with the same uses as in the present application (treatment of conditions due to the presence of Helicobacter pylori (Hp) such as gastritis, ulcers, gastric adenocarcinoma, non-Hodgkin lymphoma of human stomach, liver disease, heart disease and sudden infant death syndrome; identification of bacterial adhesions; production of a Hp vaccine; diagnosis of Hp infections; typing of Hp; identifications of Hp binding substances; inhibition of Hp binding). The compounds in D1 contain the disaccharide sequence Gal β 4Glc which the present application is based upon, though the focus in D1 lies on the sequences Gal β 3GlcNAc and Gal β 3GalNAc as binding epitopes. Specific examples are shown in Table II on pages 52-53, e.g. Gal β 3GlcNAc β 3Gal β 4Glc β 1Cer.

D2 describes Gal β 4Glc β 1Cer (lactosylceramide), Gal α 3Gal β 4Glc β 1Cer and Gal β 3GalNAc β 4Gal β 4Glc β 1Cer with binding specificity for Hp. The sequence Gal β 4Glc, or at least Gal β 4Glc β 1Cer, is thus known as a Hp binding epitope from D2.

D1 and D2 represent the closest prior art. The present invention can be regarded as solving the general problem of finding alternative Hp-binding substances.

Claims 1-2 and 13 cover compounds which differ from the examples in D1 (Table II, pages 52-53) and from the compounds in D2 only in that, for example, GalNac is substituted for Gal.

Claims 14-26, 31-32, 34-36, 39-40, 51-52 and 54-56, all dependent on claim 1 and subsequent claims, are found to contain only matters which are either routine practices or relate to the medical and nutritional use of Hp-binding compounds as known from the prior art of D1.

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Previous supplemental box.

Claims 37 and 50 cover compounds which differ from the examples in D1 and from the compounds in D2 only in that GlcNAc is substituted for the Glc β 1-bound to Cer.

Claim 38 cover compounds which differ from the examples in D1 only in that Glc is substituted for the GlcNAc β 3-bound to Gal β 4Glc β 1Cer and from the compounds in D2 only in that Glc is substituted for Gal (e.g. in Gal α 3Gal β 4Glc β 1Cer).

Claim 49 cover compounds which differ from the examples in D1 only in that another monosaccharide GalNAc, GlcNAc, Gal or Glc is inserted between GlcNAc β 3Gal β 4Glc β 1 and Cer.

The modifications mentioned above are considered to be minor manipulations of the known binding epitopes and to be obvious alternatives for the person skilled in the art, looking for solutions to the above mentioned problem. The person skilled in the art would expect retention of biological activity for these modifications. For example, that the difference between Gal α 3Gal β 4Glc β 1Cer and Glc α 3Gal β 4Glc β 1Cer probably is insignificant with regard to binding activity can be justified by comparing with D1 (page 7, lines 3-10), in which Gal β 3GlcNAc and Gal β 3GalNAc are regarded as substantially interchangeable due to their structural similarity. For these reasons, and considering the broadness of the claims, the invention according to claims 1-2, 13-26, 31-32, 34-40, 49-56 is considered to lack an inventive step with regard to D1 or D2.

D3 describes a structure containing Gal β 4GlcA. The invention according to claims 1, 13, 18, 20-22, 25-26, 36 and 65 lacks novelty with regard to D3. This can be avoided, for example in claim 65 if the phrase "and A indicates a glucuronamide" is inserted after the phrase "q2 is 1 and r2 is 0". Note that the claims mentioning Hp are phrased as first medical indications and thereby are to be interpreted as directed to the compounds for medical use in general, with no special regard to their Hp-binding activity.

.../...

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/FI 2003/000039

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of: Previous supplemental box.

D4 describes GalNAc α 4GlcA β 3GalNAc β 4GlcA β 3Gal β 3Gal β 4Xyl (the relevant part of the structure underlined). The invention according to claims 1, 3, 5, 8, 11, 13-14, 21-22, 25-26 and 36 lacks novelty with regard to D4. Se above concerning the first medical indication.

D5 describes a structure containing two terminal GalNAc β 4GlcNAc-units β 2-bound to Man. The invention according to claims 1, 14, 21-22, 25-26 and 36 lacks novelty with regard to D5. Se above concerning the first medical indication.

D6-D14 only describe the general state of the art and are of no particular relevance.

The inventions defined in claims 4, 6-7, 9-10, 12 and 61-64 are not disclosed by any of the above documents, and are not obvious to a person skilled in the art. Accordingly, the inventions defined in claims 4, 6-7, 9-10, 12 and 61-64 are novel and are considered to involve an inventive step.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/FI 2003/000039

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 02056893 A1	25.07.2002	18.01.2002	19.01.2001

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)

STN International, File CAPLUS, CAPLUS accession no. 2002:390032, document no. 138:1587,
 Chandrasekaran, E. et al, "Biosynthesis of the carbohydrate antigenic determinants, Globo E, blood group H, and Lewis b: a role for prostate cancer cell alpha1,2-L-fucosyltransferase" & Glycobiology (2002), 12(3), 153-162

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/FI 2003/000039

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Formula 9 in the original claim 36 has been deleted in the corresponding amended claim 37.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITYInternational application No.
PCT/FI 2003/000039**Box No. VIII Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

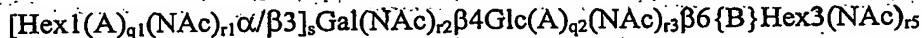
In the summary of the invention (page 3 of the description) is explained that "y is either alpha or beta indicating the anomeric structure of the terminal monosaccharide residue". Accordingly, Hex1 in claim 1, Glc(A)_{q1}(NAC)_{r1}β3 in claim 4, Glcβ3 in claims 9-10, GlcNAcβ3 in claim 10, Glc(A)_q(NAC)_rα3/β3 in claim 38 and Gal(A)_q(NAC)_r/Glc(A)_q(NAC)_rα3/β3 in claim 41 are intended to be terminal monosaccharide residues. This seems to be a relevant feature of the invention and should therefore be indicated in said independent claims. The present claims 1, 4, 9-10, 38, 41 and the respective dependent claims include non-terminal sequences.

What is claimed:

1. A *Helicobacter pylori* binding substance comprising oligosaccharide sequence
5 $[\text{Hex1(A)}_{q1}(\text{NAc})_{r1}\alpha/\beta3]_s\text{Gal}(\text{NAc})_{r2}\beta4\text{Glc(A)}_{q2}(\text{NAc})_{r3}$
wherein q1, q2, r1, r2, r3, and s are each independently 0 or 1 so that at least r2 or q2
is 1;
10 Hex1 is galactose (Gal), glucose (Glc) or mannose (Man);
and analogs or derivatives of said oligosaccharide sequence having binding activity
to *Helicobacter pylori* for the prophylaxis or treatment of any condition due to the
presence of *Helicobacter pylori* in a subject.
- 15 2. The *Helicobacter pylori* binding substance according to claim 1 further
comprising $\beta6\text{Hex3}(\text{NAc})_{r5}$ or $\beta3\text{Hex3}(\text{NAc})_{r5}$ structure in the reducing end of the
oligosaccharide sequence forming the following structure
20 $[\text{Hex1(A)}_{q1}(\text{NAc})_{r1}\alpha/\beta3]_s\text{Gal}(\text{NAc})_{r2}\beta4\text{Glc(A)}_{q2}(\text{NAc})_{r3}\beta6/\beta3\text{Hex3(A)}_{r4}(\text{NAc})_{r5}$
wherein q1, q2, r1, r2, r3, s, and Hex1 are as defined in claim 1; r4 and r5 are
independently 0 or 1; Hex3 is mannose (Man), galactose (Gal) or glucose (Glc).
- 25 3. The *Helicobacter pylori* binding substance according to claim 2, wherein said
oligosaccharide sequence is according to structure
 $\text{Glc(A)}_{q1}(\text{NAc})_{r1}\beta3\text{Gal}\beta4\text{Glc(NAc)}_{r3}\beta6\text{Hex3}(\text{NAc})_{r5}$
30 wherein q1, r1, and r3 are as defined in claim 1; r5 and Hex3 are as defined in claim
2.
- 35 4. The *Helicobacter pylori* binding substance according to claim 1 further
comprising $\beta3\text{Gal}(\text{NAc})_{r5}[\beta4\text{Glc(A)}_{q3}(\text{NAc})_{r6}]_u$ structure in the reducing end of the
oligosaccharide sequence forming the following structure
 $[\text{Hex1(A)}_{q1}(\text{NAc})_{r1}\alpha/\beta3]_s\text{Gal}(\text{NAc})_{r2}\beta4\text{Glc(A)}_{q2}(\text{NAc})_{r3}\beta3\text{Gal}(\text{NAc})_{r5}[\beta4\text{Glc(A)}_{q3}(\text{NAc})_{r6}]_u$

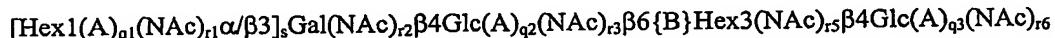
wherein q1,q2, r1, r2, r3, s, and Hex1 are as defined in claim 1; r5 is as defined in claim 2, q3, r6, and u are independently 0 or 1.

5. The *Helicobacter pylori* binding substance according to claim 1 further comprising $\beta 6\{B\}Hex3(NAc)_{r5}$ structure in the reducing end of the oligosaccharide sequence forming the following structure



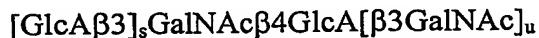
10 wherein q1,q2, r1, r2, r3, s, and Hex1 are as defined in claim 1; B is branch structure $Hex2(NAc)_{r4}\beta3$, Hex2 and Hex 3 are independently mannose (Man), galactose (Gal) or glucose (Glc), r5 is independently 0 or 1.

15 6. The *Helicobacter pylori* binding substance according to claim 1 further comprising $\beta 6\{B\}Hex3(NAc)_{r5}[\beta4Glc(A)_{q3}(NAc)_{r6}]_u$ structure in the reducing end of the oligosaccharide sequence forming the following structure



20 wherein q1,q2, r1, r2, r3, s, and Hex1 are as defined in claim 1; B is as defined in claim 4, q3 and r6 are independently 0 or 1.

25 7. The *Helicobacter pylori* binding substance according to claim 1, wherein said oligosaccharide sequence is a natural type chondroitin sequence according to the following structure

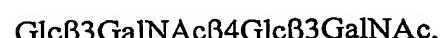


wherein s and u are as defined above with the proviso that either s or u is 1.

30 8. The *Helicobacter pylori* binding substance according to claim 1 comprising one or several of the following oligosaccharide sequences



35 $Glc\beta3GalNAc\beta4Glc\beta3GalNAc\beta4Glc,$
 $Glc\beta3GalNAc\beta4Glc\beta3GalNAc\beta4Glc\beta3GalNAc\beta4Glc,$



Glc β 3GalNAc β 4Glc β 3GalNAc β 4Glc β 3GalNAc β 4Glc β 3GalNAc,

Glc β 3GlcNAc β 4Glc,

Glc β 3GlcNAc β 4Glc β 3GlcNAc β 4Glc,

5 Glc β 3GlcNAc β 4Glc β 3GlcNAc β 4Glc β 3GlcNAc β 4Glc,

Glc β 3GlcNAc β 4Glc β 3GlcNAc,

Glc β 3GlcNAc β 4Glc β 3GlcNAc β 4Glc β 3GlcNAc, and

Glc β 3GalNAc β 4Glc β 3GlcNAc β 4Glc β 3GlcNAc β 4Glc β 3GlcNAc

10 9. The *Helicobacter pylori* binding substance according to claim 2 comprising one or several of the following oligosaccharide sequences

GlcNAc β 3Gal β 4GlcNAc β 6GlcNAc,

Glc β 3Gal β 4GlcNAc β 6GlcNAc,

15 GlcA β 3Gal β 4GlcNAc β 6GlcNAc,

GlcNAc β 3Gal β 4GlcNAc β 6GalNAc,

Glc β 3Gal β 4GlcNAc β 6GalNAc,

GlcA β 3Gal β 4GlcNAc β 6GalNAc,

GlcNAc β 3Gal β 4GlcNAc β 6Gal,

20 Glc β 3Gal β 4GlcNAc β 6Gal, and

GlcA β 3Gal β 4GlcNAc β 6Gal.

10. The *Helicobacter pylori* binding substance according to claim 1 comprising one or several of the following oligosaccharide sequences

25

GlcA β 3GalNAc β 4GlcA,

GlcA β 3GalNAc β 4GlcA β 3GalNAc β 4GlcA,

GlcA β 3GalNAc β 4GlcA β 3GalNAc β 4GlcA β 3GalNAc β 4GlcA, and

GlcA β 3GalNAc β 4GlcA β 3GalNAc β 4GlcA β 3GalNAc β 4GlcA β 3GalNAc β 4GlcA

30

11. The *Helicobacter pylori* binding substance according to claim 1 comprising one or several of the following oligosaccharide sequences

35 GalNAc β 4GlcA β 3GalNAc β 4GlcA,

GalNAc β 4GlcA β 3GalNAc β 4GlcA β 3GalNAc β 4GlcA,

GalNAc β 4GlcA β 3GalNAc β 4GlcA β 3GalNAc β 4GlcA β 3GalNAc β 4GlcA,

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ART 4(4)(B)
GalNAc β 4GlcA β 3GalNAc,

GalNAc β 4GlcA β 3GalNAc β 4GlcA β 3GalNAc, and

GalNAc β 4GlcA β 3GalNAc β 4GlcA β 3GalNAc β 4GlcA β 3GalNAc

5

12. The *Helicobacter pylori* binding substance according to claim 1 comprising at least one of the following oligosaccharide sequence

GalNAc β 4Glc,

10 Gal β 4GlcA, and

GalNAc β 4GlcA

15 13. The *Helicobacter pylori* binding substance according to any one of claims 1 – 12, wherein the substance is conjugated to a polysaccharide, preferably to a polylactosamine chain or a conjugate thereof.

14. The *Helicobacter pylori* binding substance according to any one of claims 1 – 12, wherein the substance is a glycolipid.

20 15. The *Helicobacter pylori* binding substance according to any one of claims 1 – 12, wherein the substance is an oligomeric molecule containing at least two or three oligosaccharide chains.

25 16. The *Helicobacter pylori* binding substance consisting of a micelle comprising one or more of the substances of any one of claims 1 – 15.

17. The *Helicobacter pylori* binding substance according to any one of claims 1 – 16, wherein the substance(s) is/are conjugated to a carrier.

30 18. The *Helicobacter pylori* binding substance according to any one of claims 1 - 17, wherein the substance is covalently conjugated with an antibiotic effective against *Helicobacter pylori*, preferably a penicillin type antibiotic.

35 19. The *Helicobacter pylori* binding substance or a mixture of substances according to any one of claims 1 – 17, wherein position C1 of reducing end terminal Glc or GlcNAc of the oligosaccharide sequence (OS) is oxygen linked ($-O-$) to an oligovalent or a polyvalent carrier (Z), via a spacer group (Y) and optionally via a monosaccharide or oligosaccharide residue (X), forming the following structure

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[OS -O- (X)_n - Y]_m - Z

where integers m, and n have values m ≥ 1, and n is independently 0 or 1; X is preferably lactosyl-, galactosyl-, poly-N-acetyl-lactosaminyl, or part of an O-glycan

5 or an N-glycan oligosaccharide sequence, Y is a spacer group or a terminal conjugate such as a ceramide lipid moiety or a linkage to Z;

or an analog or a derivative of the substance of said structure having binding activity to *Helicobacter pylori*.

10

20. The substance according to any one of claims 1 - 19 for use as a *Helicobacter pylori* binding or inhibiting substance.

21. The substance according to any one of claims 1 - 19 for use as a medicament.

15

22. Use of the substance according to any one of claims 1 - 19 for the production of a composition having *Helicobacter pylori* binding or inhibiting activity.

20

23. Use of the substance according to any one of claims 1 - 19 for the production of a pharmaceutical composition for the treatment of any condition due to the presence of *Helicobacter pylori*.

25

24. A pharmaceutical composition comprising the substance according to any one of claims 1 - 19 for the treatment of any condition due to the presence of *Helicobacter pylori*.

30

25. The pharmaceutical composition according to claim 24, for the treatment of chronic superficial gastritis, gastric ulcer, duodenal ulcer, gastric adenocarcinoma, non-Hodgkin lymphoma in human stomach, liver disease, pancreatic disease, skin disease, heart disease, or autoimmune diseases including autoimmune gastritis and pernicious anaemia and non-steroid anti-inflammatory drug (NSAID) related gastric disease, or for prevention of sudden infant death syndrome.

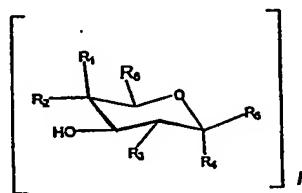
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26. A method for the treatment of a condition due to presence of *Helicobacter pylori*, wherein a pharmaceutically effective amount of the substance according to any one of claims 1 - 19 or the composition according to claims 24 or 25 is administered to a subject in need of such treatment.

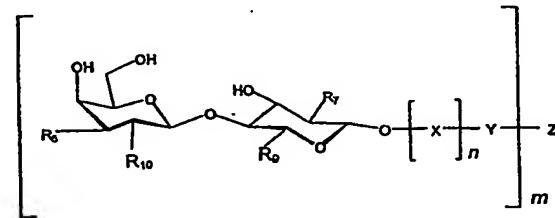
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27. The method according to claim 26, when said condition is caused by the presence of *Helicobacter pylori* in the gastrointestinal tract of a patient.
28. The method according to claim 26, for the treatment of chronic superficial gastritis, gastric ulcer, duodenal ulcer, gastric adenocarcinoma, non-Hodgkin lymphoma in human stomach, liver disease, pancreatic disease, skin disease, heart disease, or autoimmune diseases including autoimmune gastritis and pernicious anaemia and non-steroid anti-inflammatory drug (NSAID) related gastric disease, or for prevention of sudden infant death syndrome.
- 10 29. Use of the substance according to any one of claims 1 - 19, for the diagnosis of a condition due to infection by *Helicobacter pylori*.
- 15 30. A nutritional additive or composition containing the substance according to any one of claims 1 - 19.
31. The nutritional additive or composition according to claim 30 for use in infant food.
- 20 32. Use of the substance according to any one of claims 1 - 19, for the identification of bacterial adhesin.
33. Use of the substance according to any one of claims 1 - 19 or a substance identified according to claim 32, for the production of a vaccine against
- 25 *Helicobacter pylori*.
34. Use of the substance according to any one of claims 1 - 19, for typing *Helicobacter pylori*.
- 30 35. The substance according to any one of claims 1 - 19, for use in *Helicobacter pylori* binding assays.
36. A *Helicobacter pylori* binding substance comprising an oligosaccharide sequence according to Formula 9

35



A-saccharide

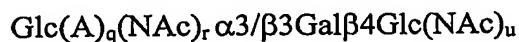


B-saccharide

wherein integers l, m, and n have values m = 1, l and n are independently 0 or 1; R₁ is H and R₂ is OH, or R₁ is OH and R₂ is H, or R₁ is H and R₂ is a monosaccharidyl- or oligosaccharidyl- group, preferably a beta glycosidically linked galactosyl group, R₃ is independently -OH or acetamido (-NHCOCH₃) or an acetamido analogous group, R₇ is acetamido (-NHCOCH₃) or an acetamido analogous group; when l = 1, R₄ is -H and R₅ is oxygen linked to bond R₆ and forms a beta anomeric glycosidic linkage to saccharide B, or R₅ is -H and R₄ is oxygen linked to bond R₆ and forms an alpha anomeric glycosidic linkage to saccharide B; when l = 0, R₆ is -OH linked to B; X is monosaccharide or oligosaccharide residue, X is lactosyl-, galactosyl-, poly-N-acetyl-lactosaminyl, or part of an O-glycan or an N-glycan oligosaccharide sequence; Y is a spacer group or a terminal conjugate such as a ceramide lipid moiety or a linkage to Z; Z is an oligovalent or a polyvalent carrier; the oxygen linkage (-O-) between position C1 of the B saccharide and saccharide residue X or spacer group Y can be replaced by carbon (-C-), nitrogen (-N-) or sulphur (-S-) linkage; R₈ and R₉ are independently carboxylic acid amide, such as methylamide or ethylamide, hydroxymethyl (-CH₂-OH) or a carboxylic acid group or an ester thereof, such as methyl or ethyl ester; R₃, R₇, and R₁₀ are independently hydroxyl, acetamido or acetamido group mimicking group, such as C₁₋₆ alkyl-amides, arylamido, secondary amine, preferentially N-ethyl or N-methyl, O-acetyl, or O-alkyl for example O-ethyl or O-methyl.

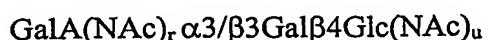
37. A *Helicobacter pylori* binding substance comprising an oligosaccharide sequence

25



wherein q, r and u are independently 0 or 1,

30 with the proviso that when said oligosaccharide sequence contains $\beta 3$ linkage, both q and r are 0 or 1; or



35 wherein r and u are independently 0 or 1, and *Helicobacter pylori* binding analogs and derivatives thereof.

38. A *Helicobacter pylori* binding non-acidic polyvalent substance comprising the oligosaccharide sequence as defined in any one of claims 1-18, wherein said oligosaccharide sequence (OS) is a part of structure

5 [OS -O- (X)_n - Y]_m - Z

as defined in claim 19, Y being a hydrophilic spacer, more preferably a flexible hydrophilic spacer, and *Helicobacter pylori* binding analogs and derivatives thereof.

10 39. The *Helicobacter pylori* binding non-acidic polyvalent substance according to claim 38, wherein linker structure Y is

[OS -O- (X)_n-L₁-CH(H/{CH₁₋₂OH}_{p1}) - {CH₁OH}_{p2}- {CH(NH-R)}_{p3} - {CH₁OH}_{p4} - L₂]_m-Z

15 wherein L₁ and L₂ are linking groups comprising independently oxygen, nitrogen, sulphur or carbon linkage atom or two linking atoms of the group forming linkages such as -O-, -S-, -CH₂-, -N-, -N(COCH₃)-, amide groups -CO-NH- or -NH-CO- or -N-N- (hydrazine derivative) or an amino oxy-linkages -O-N- and -N-O-; L₁ is linkage from carbon 1 of the reducing end monosaccharide of X or when n =0, L₁ replaces -O- and links directly from the reducing end C1 of OS; p1, p2, p3, and p4 are independently integers from 0-7, with the proviso that at least one of p1, p2, p3, and p4 is at least 1; CH₁₋₂OH in the branching term {CH₁₋₂OH}_{p1} means that the chain terminating group is CH₂OH and when the p1 is more than 1 there is secondary alcohol groups -CHOH- linking the terminating group to the rest of the spacer; R is preferably acetyl group (-COCH₃) or R is an alternative linkage to Z and then L₂ is one or two atom chain terminating group, in another embodiment R is an analog forming group comprising C₁₋₄ acyl group comprising amido structure or H or C₁₋₄ alkyl forming an amine; and m > 1 and Z is polyvalent carrier; OS and X are as defined in claim 12.

30

40. A *Helicobacter pylori* binding substance comprising the oligosaccharide sequence



wherein q, r and u are each independently 0 or 1, with the proviso that said oligosaccharide sequence is not Gal α 3Gal β 4Glc/GlcNAc,

5 as a non-reducing end terminal sequence, and *Helicobacter pylori* binding analogs and derivatives thereof.

41. The substance according to any one of claims 37-40 for use in binding bacteria, toxins or viruses.

10

42. The substance according to any one of claims 37-40 for use as a medicament.

15

43. A method for the treatment of a condition due to presence of *Helicobacter pylori*, wherein a pharmaceutically effective amount of the substance as defined in any one of claims 1 – 19 or 37-40 is administered to a subject in need of such treatment.

44. The method according to claim 43, when said condition is caused by the presence of *Helicobacter pylori* in the gastrointestinal tract of a patient.

20

45. The method according to claim 43, for the treatment of chronic superficial gastritis, gastric ulcer, duodenal ulcer, gastric adenocarcinoma, non-Hodgkin lymphoma in human stomach, liver disease, pancreatic disease, skin disease, heart disease, or autoimmune diseases including autoimmune gastritis and pernicious anaemia and non-steroid anti-inflammatory drug (NSAID) related gastric disease, or for prevention of sudden infant death syndrome.

25

46. The method of treatment according to any one of claims 43-45, wherein said substance is a nutritional additive or a part of a nutritional composition.

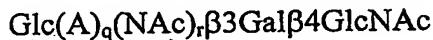
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47. The substance according to claim 41, wherein said toxin is toxin a of *Clostridium difficile*.

48. The substance according to any one of claims 40-42, wherein said oligosaccharide sequence is β 1-6 linked from the reducing end to GalNAc, GlcNAc, Gal or Glc.

35

49. The substance according to any one of claims 40-42, wherein said oligosaccharide sequence is



5

q and r being as defined in claim 40.

50. A method of screening *Helicobacter pylori* binding substances comprising

10 - modifying at least one hydroxyl or acetamido group of an oligosaccharide sequence as defined in any one of claims 1-19 into another chemical group

- determining *Helicobacter pylori* binding or inhibiting substances from the modified oligosaccharide sequences

15

51. A functional food comprising substances according to any of the claims 1-19 or 40.

20

52. A functional food comprising substances according to any of the claims 8-12

53. A functional food according to claim 51 or 52, wherein said food is a beverage.

54. A functional food according to claim 51 or 52, wherein said food is an infant formula.

25

55. A functional food according to claim 51 or 52, wherein said food is animal feed.

56. A method of producing chondroitin oligosaccharides from chondroitin sulphates comprising

30 - removing sulphates from chondroitin sulphate by chemical hydrolysis
- specifically hydrolyzing glycosidic bonds between GalNAc and GlcA

35 57. The method of claim 56, wherein the hydrolysis is performed by acid hydrolysis, preferably by a strong carboxylic acid.

58. The method of claim 56, wherein said strong carboxylic acid is trifluoroacetic acid.

59. The method of claim 56 further comprising a step of purification involving anion exchange chromatography and/or gel filtration chromatography (size exclusion chromatography).

5

60. A method for production of amidated glucuronic acid comprising oligosaccharides and monosaccharides from glucuronic acid comprising polysaccharides, the method comprising the steps of

10

- optionally oxidating of 6-hydroxyls of a polysaccharide to carboxylic acid groups,
- when the substrate does not comprise uronic acid groups, or does contain oxidatable 6-hydroxyl groups.
- amidating of glucuronic acid residues of the glucuronic acid comprising polysaccharide
- hydrolysing the polysaccharide to fragments
- optionally isolating oligosaccharide by chromatographic means.

15

61. The method according to claim 60, wherein said polysaccharides are selected from the group consisting of pectin, desulphated chondroitin sulphate, hyaluronic acid and bacterial exopolysaccharide comprising glucuronic acid.

20

62. The method according to claim 60, wherein the amidation is performed from the polysaccharide activated by uronium type amide bond synthesis activator.

63. The method according to claim 60, wherein the carboxylic acid is activated by methyl ester.

25

64. The method according to claim 60, wherein said fragments are either oligosaccharides or monosaccharides.

30

65. Helicobacter pylori binding substance
 $[Hex1(A)_{q1}(NAc)_{r1}y3]_{s1}Gal(NAc)_{r2}\beta4Glc(A)_{q2}(NAc)_{r3}$

35

wherein q1,q2, r1, r2, r3, and s1, are each independently 0 or 1, and Hex1, and Hex2 is a hexose structures, preferably galactose (Gal) or glucose (Glc), which may be further modified by the A and/or NAC groups; y is either alpha or beta indicating the anomeric structure of the terminal monosaccharide residue with the provisions that at least r2 is 1 or q2 is 1 and that A indicates a glucuronamide when at least q1 or q2 is 1

or when s1 is 0, then

q2 is 1 and r2 is 0

or q2 and r2 and r3 are 1

or q2 and r2 are 1, r3 is 0 and A indicates a glucuronamide;

5 or when s is 1 then when r2 is 1 then at least q1 is 1 or q2 is 1

with the provision that the molecule does not comprise two non-derivatized β -linked
glucuronic acid units.

66. A method of screening *Helicobacter pylori* binding substance analogs

10 comprising

-docking by molecular modeling a carbohydrate binding molecule of *Helicobacter pylori* *in silico*

15 -designing binding active analogues by allowing determination of binding interactions and positions for possible additional binding interactions

- determining *Helicobacter pylori* binding or inhibiting substances from the modified carbohydrate binding molecules

67. The method according to claim 66, wherein said carbohydrate binding molecule

20 of *Helicobacter pylori* is a *Helicobacter pylori* binding oligosaccharide sequence according to claim 1.